

JUN 14 2002

RECEIVED

REMARKS**I. RESTRICTION REQUIREMENT**

Claims 1-15 are pending in this application. The Office Action required restriction from among:

Group I: Claims 1-7, drawn to a method of treating a disorder by implanting a cell matrix comprising cells that express a gene encoding an anti-angiogenic molecule, classified in class 514, subclass 44; and

Group II: Claims 8-15, drawn to a cell matrix structure, classified in class 424, subclass 93.1.

Group I is elected with traverse for further prosecution in this application.

Reconsideration and withdrawal of the restriction requirement are respectfully requested in view of the remarks herewith.

As a traverse, it is noted that the claims of Group II are directed to a cell matrix structure, and those of Group I are directed to methods of using the cell matrix structure of Group II. Therefore, these groups should be rejoined into this application at this time, pursuant to MPEP 821.04. Furthermore, the present claims represent a web of knowledge and continuity of effort that merits examination in a single application. In this regard, the Examiner is respectfully requested to review MPEP § 808.02 which states, "... even with patently distinct inventions, restriction is not (emphasis added) required unless one of the following reasons appears:

1. Separate classification;
2. Separate status in the art; or
3. Different field of search ..."

Additionally, the Examiner's attention is further respectfully invited to review the text of MPEP § 803 which in part states:

If the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to distinct or independent inventions (emphasis added).

Contrary to the guidelines mandated by the MPEP, the claims of the two groups do not have separate status in the art, nor do they include different fields of search. The groups have been classified in different classes, but arguably so. All of the claims in both groups involve a cell matrix structure. In fact, the independent claim of Group I, claim 1, contains the exact same

recitation as the independent claim of Group II, claim 8. It is difficult to imagine how a search of the Group I claims for the method of treating a disorder using the cell-matrix structure described in the Group II claims could not encompass the subject matter of both groups.

In sum, Groups I and II can be searched and examined in this application as there is no undue or serious burden in searching and examining these claims together. On the contrary, enforcing the present restriction requirement would result in inefficiencies and unnecessary expenditures by both the Applicants and the PTO, as well as extreme prejudice to Applicants (particularly in view of GATT, whereby a shortened patent term may result in any divisional applications filed). Restriction has not been shown to be proper, especially since the requisite showing of serious burden has not been made in the Office Action and there are relationships between the claims of both Groups. The art, search and examination of Group I will necessarily encompass the subject matter of Group II. Thus, search and examination of all of the claimed subject matter can be made without any undue or serious burden on the Examiner. All of the preceding, therefore, direct against restriction.

II. CLAIM FOR PRIORITY

The Office Action alleges that provisional application No. 60/127,221 (“the ‘221 application”), to which this application claims priority, does not provide adequate support for the present claims. Applicants respectfully traverse the Examiner’s assessment of the ‘221 application. The ‘221 application discloses a method of treating a subject with a disorder characterized by unwanted cell proliferation by increasing expression of an anti-angiogenic molecule, TSP-2. As disclosed on pages 5 and 18 of the ‘221 application, this can be accomplished by introducing into the subject a genetically modified cell that expresses the molecule. Thus, the subject matter of the instant application—using a cell-matrix structure as a delivery vehicle—is present in the ‘221 application. Furthermore, the ‘221 application does not limit the method by which such cells are introduced into a subject. The ‘221 application states on page 39 that the gene therapy construct “can comprise a slow release matrix in which the gene delivery vehicle is imbedded.” Such a matrix is analogous to that of the instant invention. Therefore, both the concept of an implantable matrix and that of introducing a genetically modified cell or cells are disclosed in the ‘221 application, which provides adequate support for the full scope of the claims of the instant application.

III. THE REJECTION UNDER 35 U.S.C. §112 IS OVERCOME

Claim 2 was rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is respectfully submitted that the present application does enable one of skill in the art to make and use the claimed invention and the rejection is traversed.

The Office Action alleges that the specification does not provide enablement for the use of anti-angiogenic molecules in the treatment of disorders not due to overexpression of angiogenic factors and that there is no teaching in the art disclosing the same. As the enclosed references demonstrate, angiogenesis does play a role in disorders other than tumor growth. Detmar *et al.* (J. Exp. Med., 1994) (Tab 1) showed a role for angiogenic factors in psoriasis. Jackson *et al.* (Inflamm. res. Supp. 1997) (Tab 2) showed that inhibitors of angiogenesis modulated cytokines associated with chronic inflammatory disease, such as rheumatoid arthritis. Jackson *et al.* (FASEB 1997) (Tab 3) also discussed the codependence of angiogenesis and chronic inflammation. Therefore, conditions characterized by excessive proliferation of cells have been linked to angiogenesis, and this information was available in several references at the time the instant application was filed. One of skill in the art would have been able to use to the methods of the invention to treat the disorders disclosed in the application and claimed in claim 2. In view of the knowledge in the art evidenced by the references cited herein, reconsideration and withdrawal of the § 112, first paragraph, rejection is solicited.

IV. THE REJECTION UNDER 35 U.S.C. §103 IS OVERCOME

Claims 1-7 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Vacanti *et al.*, in view of Locopo *et al.* and Streit *et al.* The rejection is traversed. The publication by Streit *et al.* is not prior art under 35 U.S.C. § 102(a), as it is not the work of others. Attached is a Declaration in accordance with M.P.E.P. § 2132.01 attesting to this fact (Tab 4). The Declaration is executed by the individuals who are both authors of the publication by Streit *et al.* and inventors named in the instant application. Streit *et al.* is also not prior art under 35 U.S.C. 102(b), as it was published in the December 21, 1999 issue of the *Proceedings of the National Academy of Sciences USA*, i.e., not more than one year before the priority date of this application. As addressed above, the instant application is entitled to a priority date of

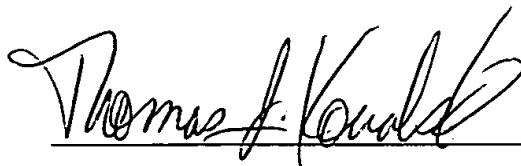
March 31, 1999. However, even if Applicants are denied that date, the March 24, 2000 filing date of U.S.S.N. application serial No. 09/536,087, to which the instant application properly claims priority, is still within one year of the publication date of the Streit *et al.* reference. None of the other paragraphs of § 102 apply to the Streit *et al.* reference. Therefore, Streit *et al.* cannot be considered prior art under 35 U.S.C. § 102, and cannot be used to support a rejection under 35 U.S.C. § 103. Consequently, reconsideration and withdrawal of the § 103 rejection are requested.

CONCLUSION

In view of the remarks and amendments herewith, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorneys for Applicant

A handwritten signature in black ink, appearing to read "Thomas J. Kowalski", written over a horizontal line.

Thomas J. Kowalski
Reg. No. 32,147
Tel: (212) 588-0800